

**Magellan Rx**  
MANAGEMENT<sup>SM</sup>

Magellan Medicaid  
Administration

# Washington Drug Utilization Review (DUR) Board Meeting

June 15<sup>th</sup>, 2022

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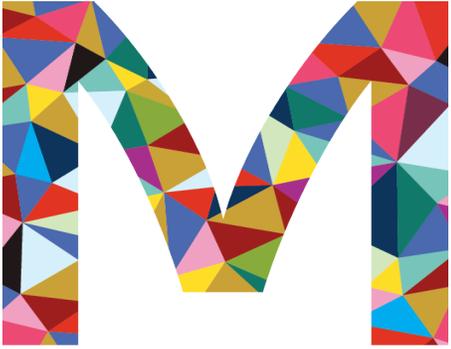
# Agenda Topics

Overview of Disease  
State

Indications

Dosage & Formulations

Guideline Updates



## COPD Agents

- Asthma and COPD Agents: Anticholinergics
- Asthma and COPD Agents: Phosphodiesterase 4 Inhibitors
- Asthma and COPD Agents: Long-Acting Muscarinic Agent/Long-Acting Beta Agonist Combinations
- Asthma and COPD Agents: Long-Acting Muscarinic Agents



## Glucocorticoids, Inhaled

- Asthma and COPD Agents: Inhaled Corticosteroid Combinations
- Asthma and COPD Agents: Inhaled Corticosteroid



# Disease State Description - Glucocorticoids, Inhaled

- Prevalence of asthma in the United States (US) continues to rise
  - More than 25 million Americans have asthma, and over 5 million of these are children
- The National Asthma Education and Prevention Program (NAEPP) has defined asthma as a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role
  - In susceptible individuals, inflammation may cause recurrent episodes of wheezing, breathlessness, chest tightness, and coughing
  - These episodes are usually associated with airflow obstruction that is often reversible, either spontaneously or with treatment
  - The inflammation also causes an increase in bronchial hyper-responsiveness to a variety of stimuli
- Studies have demonstrated the efficacy of inhaled corticosteroids (ICS) in improving lung function, reducing symptoms, reducing frequency and severity of exacerbations, and improving the quality of life (QoL) of patients with asthma
  - The 2007 National Heart, Lung, and Blood Institute (NHLBI) states that inhaled glucocorticoids are currently the most effective anti-inflammatory medications for the treatment of persistent asthma
  - The 2019 GINA full report advises that all patients with asthma should receive ICS-containing controller treatment to reduce risk of serious exacerbations and to control symptoms

*Centers for Disease Control and Prevention (CDC), 2020*

# Guidelines - Glucocorticoids, Inhaled

- Global Initiative for Asthma (GINA), 2021

- The guidelines offer a control-based management plan to adjust treatment in a continuous cycle of assessment, treatment, and review of the patient's response as it relates to symptom control, future risk of exacerbations, and side effects
- Equally important in this process is identifying the patient's own goals regarding their asthma management to ensure improved outcomes
- In patients whose asthma is not adequately controlled on the preferred controller despite good adherence and correct technique, a step up in treatment may be added until control is achieved. This can be a short-term or sustained step up in therapy. If control is maintained for at least 3 months on the current regimen, treatment can be stepped down to the lowest step and dosage that maintains control
- Patients should be started on treatment based on symptoms, with infrequent symptoms beginning at Step 1 and patients with the most frequent, severe, or debilitating symptoms beginning at Step 4
- Notably, reliever therapy can be considered for symptom management prior to exercise, if needed
- The GINA 2021 guidelines describe 2 treatment tracks: Track 1 and Track 2 (next slide)
  - In Track 1, the reliever is as-needed low dose ICS-formoterol
  - In Track 2, the reliever is an as-needed SABA, which is the alternative approach when Track 1 is not an option or is not preferred for patient-specific reasons

# Guidelines - Glucocorticoids, Inhaled

- Global Initiative for Asthma (GINA), 2021

Step	Track 1	Track 2	Other Controller Options
1	<ul style="list-style-type: none"> <li>▪ As-needed low dose ICS/formoterol</li> </ul>	<ul style="list-style-type: none"> <li>▪ Low dose ICS (whenever SABA is taken)</li> <li>▪ With as-needed SABA</li> </ul>	--
2	<ul style="list-style-type: none"> <li>▪ <b>As-needed low dose ICS/formoterol</b></li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Low dose maintenance ICS</b></li> <li>▪ With as-needed SABA</li> </ul>	<ul style="list-style-type: none"> <li>▪ Low dose ICS (whenever SABA is taken) or daily LTRA or add HDM SLIT</li> </ul>
3	<ul style="list-style-type: none"> <li>▪ Low dose maintenance ICS/formoterol</li> <li>▪ With as-needed low dose ICS/formoterol</li> </ul>	<ul style="list-style-type: none"> <li>▪ Low dose maintenance ICS/LABA</li> <li>▪ With as-needed SABA</li> </ul>	<ul style="list-style-type: none"> <li>▪ Medium dose ICS or add LTRA or add HDM SLIT</li> </ul>
4	<ul style="list-style-type: none"> <li>▪ Medium dose maintenance ICS/formoterol</li> <li>▪ With as-needed low dose ICS/formoterol</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Medium/high dose maintenance ICS/LABA</b></li> <li>▪ With as-needed SABA</li> </ul>	<ul style="list-style-type: none"> <li>▪ Add LAMA or add LTRA or switch to high dose ICS</li> </ul>
5	<ul style="list-style-type: none"> <li>▪ <b>Add on LAMA</b>; refer for phenotypic assessment ± anti-IgE (omalizumab), anti-IL-5/5R (mepolizumab, reslizumab, benralizumab), anti-IL4R (dupilumab)</li> <li>▪ <b>Consider high dose ICS/formoterol</b></li> <li>▪ With as-needed low dose ICS/formoterol</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Add on LAMA</b>; refer for phenotypic assessment ± anti-IgE (omalizumab), anti-IL-5/5R (mepolizumab, reslizumab, benralizumab), anti-IL4R (dupilumab)</li> <li>▪ <b>Consider high dose ICS/LABA</b></li> <li>▪ With as-needed SABA</li> </ul>	<ul style="list-style-type: none"> <li>▪ Add azithromycin (adults) or add LTRA or add low dose oral corticosteroid (considering adverse effects)</li> </ul>

# Guidelines - Glucocorticoids, Inhaled

- American College of Chest Physicians (CHEST), 2020

- A 2020 Expert Panel Report on the management of chronic cough due to asthma and non-asthmatic eosinophilic bronchitis (NAEB) in adults and adolescents addresses the role of ICS in these patients
- For patients with chronic cough due to asthma as a unique system (cough variant asthma), they recommend ICS as first-line treatment
- If this is inadequate, the dose may be increased, treatment can be switched to a leukotriene inhibitor, or an ICS/LABA can be considered
- ICS are also recommended first-line for chronic cough due NAEB (Grade 2B), although they are not FDA- approved for this use

- National Asthma Education and Prevention Program, 2020

- Recommend a similar classification of asthma severity and control, to guide in the initiation and adjustment of therapy, respectively
- Asthma severity and control are defined in terms of 2 domains, impairment and risk
  - The distinction between these domains emphasizes the need to consider separately, asthma's effects on quality of life and functional capacity on an ongoing basis (e.g., in the present), along with risks for adverse events, such as exacerbations and progressive loss of pulmonary function
- The group recommends a step-wise approach to asthma management, which is detailed in the table below. In addition, all asthma patients should have a SABA inhaler for use on an as-needed basis
- As needed ICS with formoterol is recommended instead for patients 5 to 11 years of age at steps 3 and 4 (as low-dose or medium-dose, respectively), but a SABA is recommended as an alternative
- For combinations of an ICS and a LABA for patients  $\geq 5$  years of age, the group states a single inhaler is preferable

# Glucocorticoids, Inhaled

- **ArmonAir Respiclick (fluticasone propionate)**

- **July 2021: FDA approved for the maintenance treatment of asthma as prophylactic therapy in patients 4-11 years old. Previously, it was only approved for use in patients  $\geq 12$  years old only**

- **Indications**

- **The maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients 4 years of age and older**
- Limitations of use: Not indicated for relief of acute bronchospasm

- **Precautions**

- Primary treatment of status asthmaticus or other acute episodes of asthma requiring intensive measures
- Severe hypersensitivity to milk proteins or any ingredients

- **Dosage**

- Starting dosage is based on prior asthma therapy and disease severity
- Adult and pediatric patients 12 years and older: 1 inhalation of 55 mcg, 113 mcg, or 232 mcg twice daily by oral inhalation
- Pediatric patients 4 to 11 years of age: 1 inhalation of ARMONAIR RESPICLICK 30 mcg or 55 mcg twice daily by oral inhalation
- Do not use with a spacer or volume holding chamber

- **Availability**

- Inhalation powder: 30 mcg, 55 mcg, 113 mcg, or 232 mcg of fluticasone propionate per actuation

- **New Generic**

- Breyna (budesonide/formoterol fumarate dihydrate)- March 2022

- First FDA-approved generic for AstraZeneca's Symbicort from Mylan; product will be marketed under the trade name Breyna; launch is anticipated in 2022

# Glucocorticoids, Inhaled

- **Armonair Digihaler (fluticasone propionate)**

- **April 2022: FDA approved for the maintenance treatment of asthma as prophylactic therapy in adult and pediatric patients  $\geq 4$  years old. Previously, it was only indicated in pediatrics  $\geq 12$  years old**

- **Indications**

- **The maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older**
- Limitations of use: Not indicated for relief of acute bronchospasm

- **Precautions**

- Primary treatment of status asthmaticus or other acute episodes of asthma requiring intensive measures
- Severe hypersensitivity to milk proteins or any ingredients

- **Dosage**

- Starting dosage is based on prior asthma therapy and disease severity
- Treatment of asthma in patients  $\geq 12$  years: 1 inhalation of ArmonAir Digihaler 55 mcg, 113 mcg, or 232 mcg twice daily
- ArmonAir Digihaler contains a built-in electronic module which detects, records, and stores data on inhaler events for transmission to the mobile App

- **Availability**

- Inhalation powder containing 55 mcg, 113 mcg, or 232 mcg of fluticasone propionate per actuation



# Immunomodulators, Asthma - Asthma and COPD Agents: Monoclonal Antibodies



# Immunomodulators, Asthma

- **Dupixent (dupilumab)**

- **June 2021: FDA approved 200 mg/1.14 mL single-dose auto-injector (pre-filled pen) for use in patients  $\geq 12$  years old; was already approved as 200 mg/1.14 mL pre-filled syringe and auto-injector and 300 mg/2 mL auto-injector & pre-filled syringe**
- **October 2022: FDA has expanded the indication of add-on maintenance treatment with moderate-to-severe asthma with an eosinophilic phenotype or with oral corticosteroid dependent asthma to patients  $\geq 6$  years old (previously indicated for those  $\geq 12$  years of age)**
- **Indications**
  - **Asthma: as an add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma**
  - **Atopic Dermatitis: for the treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Can be used with or without topical corticosteroids**
  - **Chronic Rhinosinusitis with Nasal Polyposis: as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP)**
  - **Limitations of use: Not indicated for relief of acute bronchospasm or status asthmaticus**
- **Dosage**
  - **Stratified by indication, age, and weight (See TCR/PI)**
- **Availability**
  - **Injection: 300 mg/2 mL solution in a single-dose pre-filled pen; Injection: 300 mg/2 mL solution in a single-dose pre-filled syringe with needle shield**
  - **Injection: 200 mg/1.14 mL solution in a single-dose pre-filled pen; Injection: 200 mg/1.14 mL solution in a single-dose pre-filled syringe with needle shield**
  - **Injection: 100 mg/0.67 mL solution in a single-dose pre-filled syringe with needle shield**

# Immunomodulators, Asthma

- **Nucala (mepolizumab)**

- **August 2021: The FDA approved an expanded indication for the liquid formulation and SC autoinjector or syringe as add-on maintenance treatment of chronic rhinosinusitis with nasal polyps (CRSwNP) in adults  $\geq 18$  years old with inadequate response to nasal corticosteroids**
- **January 2022: The FDA has approved a new 40 mg/0.4 mL liquid formulation packaged in a safety syringe device (SDD) for use in children 6 to 11 yo with severe eosinophilic asthma. The new formulation allows Nucala to be administered to children by a caregiver or Healthcare Provider**
- **Indications**
  - Add-on maintenance treatment of adult and pediatric patients aged 6 years and older with severe asthma and with an eosinophilic phenotype
  - **Add-on maintenance treatment of adult patients 18 years and older with chronic rhinosinusitis with nasal polyps (CRSwNP).**
  - The treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA)
  - The treatment of adult and pediatric patients aged 12 years and older with hypereosinophilic syndrome (HES) for  $\geq 6$  months without an identifiable non-hematologic secondary cause
  - **Limitations of use: Not indicated for relief of acute bronchospasm or status asthmaticus**
- **Dosage**
  - **Stratified by indication and age (See TCR/PI)**
- **Availability**
  - For injection: 100 mg of lyophilized powder in a single-dose vial for reconstitution
  - Injection: 100 mg/mL, single-dose prefilled autoinjector or single-dose prefilled syringe
  - **Injection: 40 mg/0.4 mL, single-dose prefilled syringe**

# Immunomodulators, Asthma

- **Tezspire (tezepelumab-ekko)**

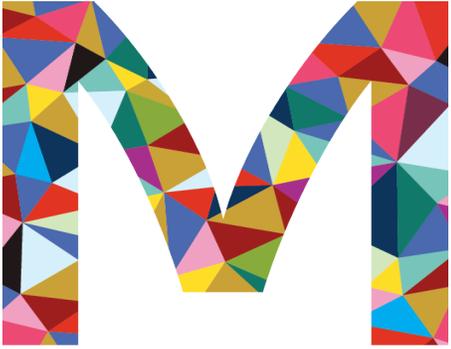
- December 2021: The FDA has approved tezepelumab-ekko (Tezspire), a thymic stromal lymphopoietin (TSLP) blocker, indicated for the add-on maintenance treatment of adult and pediatric patients aged  $\geq 12$  years with severe asthma; not for relief of acute bronchospasm or status asthmaticus
- **Indications**
  - The add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma
  - Limitations of use: Not indicated for relief of acute bronchospasm or status asthmaticus
- **Precautions**
  - Risk Associated with Abrupt Reduction in Corticosteroid Dosage: Do not discontinue systemic or inhaled corticosteroids abruptly upon initiation of therapy with TEZSPIRE. Decrease corticosteroids gradually, if appropriate
  - Parasitic (Helminth) Infection: Treat patients with pre-existing helminth infections before therapy with TEZSPIRE. If patients become infected while receiving TEZSPIRE and do not respond to antihelminth treatment, discontinue TEZSPIRE until the parasitic infection resolves
  - Vaccination: Avoid use of live attenuated vaccines
- **Dosage**
  - Administer by subcutaneous injection
  - Recommended dosage is 210 mg administered once every 4 weeks.
- **Availability**
  - Injection: 210 mg/1.91 mL (110 mg/mL) solution in a single-dose glass vial; 210 mg/1.91 mL (110 mg/mL) solution in a single-dose pre-filled syringe



# Gaucher's Disease

## - Hematopoietic Agents: Gaucher Disease





# Sickle Cell Agents

## - Hematopoietic Agents: Sickle Cell Anemia



# Disease State Description – Sickle Cell Agents

- Sickle cell disease (SCD) is an inherited red blood cell (RBC) disorder caused by a single gene mutation in the  $\beta$ -globin gene resulting in abnormal hemoglobin (Hb)
  - It affects approximately 100,000 patients in the US and is more common among African Americans, although it is also seen in people of Hispanic ancestry
  - About 1 in 365 African Americans are born with SCD, and 1 in 13 have sickle cell trait (carrier)
  - In Hispanic Americans, SCD occurs in 1 in 16,300 births
  - People with SCD have a reduced life expectancy by approximately 20 to 30 years
- People with SCD inherit 2 abnormal Hb genes, 1 from each parent
- Sickle cell disease (SCD) comprises several syndromes in which the sickle mutation is inherited along with a mutation at the other beta globin allele that diminishes or eliminates the normal production of beta globin
  - These include sickle cell anemia (homozygous sickle mutation; HbSS), sickle beta thalassemia (HbS $\beta$ ), and hemoglobin SC disease (HbSC), among others
  - There are 2 types of beta thalassemia: “0” and “+”
  - HbS $\beta$ 0 thalassemia is usually a severe form of SCD, while HbS $\beta$ + thalassemia tends to be a milder form
  - Sickle cell anemia is the most common and most severe form of SCD. Sickle cell trait (SCT) is diagnosed when one normal gene and one abnormal gene are inherited
  - Patients with SCT do not have signs or symptoms of SCD, but they can pass the abnormal gene to their children

*Centers for Disease Control and Prevention (CDC), 2020*

# Guidelines – Sickle Cell Agents

- Treatment goals in patients with SCD focus on management of symptoms and disease complications
- Strategies include management/prevention of disease sequelae, including VOC, chronic pain (managed with opioid and non-opioid analgesics), chronic hemolytic anemia, organ damage, pulmonary hypertension, stroke, and infection
- A hematopoietic cell transplant (HCT) is the only cure for SCD, but its use is limited by associated risks and lack of matched donors
  - HCT is typically performed in children with complications such as strokes
  - For treatment of acute VOCs, intravenous (IV) hydration and analgesia are the mainstay of therapy
  - Blood transfusions are often used to treat and prevent complications of SCD, particularly in patients at risk for stroke
  - However, regular administration of transfusions are associated with iron overload and alloimmunization
  - Individuals with SCD are also at increased risk for bacterial and viral infections; therefore, immunization and prophylactic penicillin are important aspects of care during early childhood (ages < 5 years)

# Respiratory – Sickle Cell Agents

- **hydroxyurea (Siklos)**

- **December 2021: FDA approved expanded indication for use in adults to reduce frequency of painful sickle cell crises and reduce need for blood transfusions; previously only indicated in pediatric patients  $\geq 2$  years old**

- **Indications**

- Reduce the frequency of painful crises and to reduce the need for blood transfusions in adult and pediatric patients, 2 years of age and older, with sickle cell anemia with recurrent moderate to severe painful crises

- **Precautions**

- BBW:

- Myelosuppression: May cause severe myelosuppression. Do not give if bone marrow function is markedly depressed. Monitor blood counts at baseline and throughout treatment. Interrupt treatment and reduce dose as necessary
- Malignancies: Hydroxyurea is carcinogenic. Advise sun protection and monitor patients for malignancies

- Embryo-Fetal toxicity: Can cause fetal harm. Advise of potential risk to a fetus and use of effective contraception

- Cutaneous vasculitic toxicities (incl. leg ulcers): Institute treatment and discontinue treatment and/or reduce dose if this occurs

- **Dosage**

- Initial dose: 15 mg/kg in adults and 20 mg/kg in children once daily. Monitor blood counts every two weeks

- The dose may be increased by 5 mg/kg/day every 8 weeks, or sooner if a severe painful crisis occurs, until a maximum tolerated dose or 35 mg/kg/day is reached if blood counts are in an acceptable range

- Discontinue treatment until hematologic recovery if blood counts are considered toxic. Resume treatment after reducing the dose by 5 mg/kg/day from the dose associated with hematological toxicity

- **Availability**

- Tablets: functionally scored 100 mg and functionally triple-scored 1,000 mg tablet

# Respiratory – Sickle Cell Agents

- **voxelotor (Oxbryta)**

- **December 2021: FDA has granted Accelerated Approval to a new formulation of voxelotor, tablets for oral suspension, for the treatment of sickle cell disease (SCD) in adults and pediatric patients  $\geq 4$  years old. Accelerated Approval is based on increase in hemoglobin (Hb); therefore, continued approval for this indication may require demonstration of benefit in confirmatory clinical trials**
- **December 2021: The existing voxelotor tablets have also received a new indication (Accelerated Approval) for the treatment of SCD in peds pts  $\geq 4$  years old. Previously, the tablet formulation was only indicated for the tx of SCD in adults and pediatric pts  $\geq 12$  years old**

- **Indications**

- **Treatment of sickle cell disease in adults and pediatric patients 4 years of age and older**

- **Precautions**

- **Laboratory Test Interference: Perform quantification of hemoglobin species when patient is not receiving treatment**

- **Dosage**

- **Adults and pediatric patients 12 years and older: 1,500 mg orally once daily**
- **Pediatric patients 4 to less than 12 years: Dosing is based on body weight**

- **Availability**

- **Tablets: 500 mg**
- **Tablets for oral suspension: 300 mg**



# Colony Stimulating Factors

- Hematopoietic Agents: Granulocyte Colony Stimulating Factors (G-CSF)



# Disease State Description - Colony Stimulating Factors

- Myelosuppressive chemotherapy can induce neutropenia (< 500 neutrophils/ $\mu$ L or < 1,000 neutrophils/ $\mu$ L and a predicted decline to  $\leq$  500/ $\mu$ L during the 48 hours after the dose) and febrile neutropenia ( $\geq$  38.3°C orally or  $\geq$  38°C sustained over 1 hour) which is a dose-limiting toxicity of chemotherapy
- Febrile neutropenia can cause increased diagnostic and treatment costs, prolonged hospitalizations, and broad-spectrum antibiotic use which may necessitate chemotherapy dose reductions, treatment delays, and may ultimately compromise treatment outcomes
- The risk of febrile neutropenia is dependent on treatment and dose intensity, which is often underreported
- Colony stimulating factors (CSF) are hematopoietic growth factors that have been shown to decrease the likelihood of neutropenic complications resulting from chemotherapy and to improve relative chemotherapy dose intensity
  - Colony stimulating factors act on hematopoietic cells and stimulate proliferation, differentiation commitment, and some end-cell functional activation
- Prophylactic CSF use can reduce the severity, risk, and duration of febrile neutropenia and decrease rates of infection and hospitalizations
  - Neupogen, Releuko, Nivestym, Zarxio, Neulasta, Nyvepria, Udenyca, Fulphila, Ziextenzo, and Granix are granulocyte colony-stimulating factors (G-CSF)
  - Leukine is a granulocyte-macrophage colony stimulating factor (GM-CSF)

*National Comprehensive Cancer Network, 2020*

# Guidelines - Colony Stimulating Factors

- **The National Comprehensive Cancer Network (NCCN) v1.2022**
  - Practice Guidelines for Hematopoietic Growth Factors in patients with solid tumors and lymphoid blood cancers
  - Due to the recent approval, pegfilgrastim-apgf (Nyvepria) and filgrastim-ayow (releuko) are not currently addressed by NCCN
  - Safety data appear similar between filgrastim (Neupogen), pegfilgrastim (Neulasta), and their biosimilars, and the subcutaneous (SC) route is preferred for all agents
  - To date, there are insufficient head-to-head comparative studies on the clinical benefits of G-CSFs and GM-CSFs
  - Subcutaneous filgrastim, tbo-filgrastim, and pegfilgrastim have a category 1 recommendation stating there is high-level evidence from randomized, controlled clinical trials, and there is uniform NCCN consensus that they prophylactically reduce the risk of febrile neutropenia. However, the guidelines advise caution should be used with prophylactic use of G-CSFs administered with chemotherapy and radiation concurrently

# Colony Stimulating Factors

- **filgrastim-ayow (Releuko)**

- **March 2022: FDA-approved biosimilar to Amgen's Neupogen (filgrastim)**

- **Indications**

- **Decrease the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a significant incidence of severe neutropenia with fever**
- **Reduce the time to neutrophil recovery and the duration of fever, following induction or consolidation chemotherapy treatment of patients with acute myeloid leukemia (AML)**
- **Reduce the duration of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in patients with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)**
- **Reduce the incidence and duration of sequelae of severe neutropenia, (e.g., fever, infections, oropharyngeal ulcers) in symptomatic patients with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia.**

- **Precautions**

- **Fatal sickle cell crises: Discontinue treatment if sickle cell crisis occurs**
- **Glomerulonephritis: Evaluate and consider dose-reduction or interruption of treatment if causality is likely**

- **Dosage**

- **Stratified by indication and weight-based dosing (See PI/TCR)**

- **Availability**

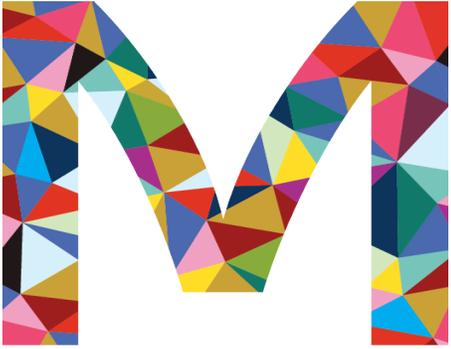
- **Vial: Injection: 300 mcg/mL in a single-dose vial; Injection: 480 mcg/1.6 mL in a single-dose vial**
- **Pre-filled Syringe: Injection: 300 mcg/0.5 mL in a single-dose prefilled syringe; Injection: 480 mcg/0.8 mL in a single-dose prefilled syringe**

# Colony Stimulating Factors

- **FDA Communication**

- Pegfilgrastim (Neulasta)- July 2021:

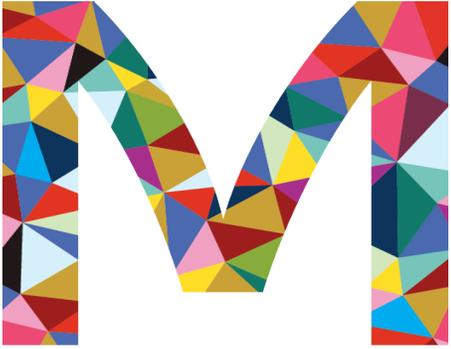
- FDA issued an untitled letter notifying Amgen of misbranding of Neulasta due to false or misleading promotional communication regarding the benefit of its Onpro system compared to traditional administration of pegfilgrastim formulations



# Erythropoiesis Stimulating Proteins

- Hematopoietic Agents: Erythropoiesis Stimulating Agents (ESAs)





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Oncology, Oral – Hematologic



# Oncology, Oral- Hematological - Overview of Disease State

- IMMUNE MODULATORS : THALIDOMIDE ANALOGUES
  - Lenalidomide
  - Pomalidomide
  - Thalidomide
  - Pomalyst
  - Revlimid
- ONCOLOGY AGENTS : ALKYLATING AGENTS - ORAL
  - Myleran
- ONCOLOGY AGENTS : ANTIMETABOLITES – ORAL
  - Onureg
  - Mercaptopurine
  - Purixan
  - Tabloid
- ONCOLOGY AGENTS : ANTINEOPLASTICS MISC – ORAL
  - Hydrea
  - Hydroxyurea
  - Matulane
- ONCOLOGY AGENTS : BCL-2 INHIBITORS – ORAL
  - Venclexta
- ONCOLOGY AGENTS : HISTONE DEACETYLASE INHIBITORS – ORAL
  - **Farydak**
  - Zolinza
- ONCOLOGY AGENTS : ISOCITRATE DEHYDROGENASE-1 (IDH1) INHIBITORS – ORAL
  - **Tibsovo**
- ONCOLOGY AGENTS : ISOCITRATE DEHYDROGENASE-2 (IDH2) INHIBITORS – ORAL
  - Idhifa
- ONCOLOGY AGENTS : JANUS ASSOCIATED KINASE (JAK) INHIBITORS – ORAL
  - Inrebic
  - Jakafi
  - **Vonjo**
- ONCOLOGY AGENTS : PHOSPHATIDYLINOSITOL 3-KINASE (PI3K) INHIBITORS – ORAL
  - Copiktra
  - **Zydelig**
- ONCOLOGY AGENTS : PROTEASOME INHIBITORS – ORAL
  - Ninlaro
- ONCOLOGY AGENTS : XPO1 INHIBITORS – ORAL
  - Xpovio

# Oncology, Oral- Hematological – Overview of Disease State

- **Graft versus Host Disease (GVHD)**

- GVHD is an immune-mediated disease that can result following hematopoietic stem cell transplant (HSCT) when the transplanted cells (graft) recognize the recipient's body as foreign
  - Organ systems most commonly impacted by acute GVHD (aGVHD) include the skin, GI tract, and liver
- Chronic GVHD (cGVHD) is generally an extension of acute GVHD that often develops more than 100 days after transplant, but it can also occur in those without acute GVHD. Symptoms include ocular manifestations (e.g., burning, irritation, photophobia, pain), oral or gastrointestinal (GI) manifestations (e.g., food sensitivity, oral dryness, pain, weight loss), respiratory manifestations (e.g., wheezing, dyspnea, cough), and neuromuscular manifestations (weakness, neuropathic pain, muscle cramps).

- **Treatment**

- The American Society for Blood and Marrow Transplantation (re-named The American Society for Transplantation and Cellular Therapy [ASTCT] in 2019) published a clinical practice guideline in 2012 around the first- and second-line treatment of aGVHD
  - These guidelines state that corticosteroids are the standard of care for the initial treatment of aGVHD and note that the literature does not support the choice of any specific agent for secondary therapy of aGVHD
  - These guidelines were published prior to the May 2019 FDA approval of ruxolitinib (Jakafi) for the treatment of corticosteroid-refractory aGVHD in adult and pediatric patients  $\geq 12$  years of age
- In 2019, the NCCN published their first set of clinical practice guidelines around hematopoietic cell transplantation (HCT)
  - The 3.2021 version of these guidelines recommend ruxolitinib as a category 1 option for patients with steroid-refractory aGVHD
- The National Institutes of Health (NIH) recommend that corticosteroids are most commonly the initial systemic therapy choice for most patients with moderate to severe cGVHD
  - Adjunctive supportive care may also be used (e.g., artificial tears, artificial saliva). Ibrutinib was the first drug approved for cGVHD in patients who have failed  $\geq 1$  systemic treatment, but many other therapies have been used off-label and for primary or secondary therapy (e.g., low-dose methotrexate, mycophenolate mofetil [CellCept], sirolimus [Rapamune])
  - The NCCN 3.2021 guidelines list ibrutinib as a category 2A recommendation for steroid-refractory cGVHD along with multiple other agents also listed as category 2A recommendations

# Oncology, Oral- Hematological – Overview of Disease State

- **Waldenström's macroglobulinemia**

- Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL) is a B-cell disorder presenting as bone marrow infiltration with lymphoplasmacytic cells that are CD19+, CD20+, and CD22+
- The 1.2022 NCCN guideline recommends treating only those patients who are symptomatic
  - These symptoms may include hyperviscosity, neuropathy, symptomatic adenopathy or organomegaly, amyloidosis, cryoglobulinemia, and cytopenias
  - Both zanubrutinib and ibrutinib with or without rituximab are listed as options for primary treatment (both category 1, preferred), while ixazomib combined with rituximab and dexamethasone is a category 2A, other recommended regimen for primary therapy
  - For patients who have received previous therapies for Waldenström's macroglobulinemia, zanubrutinib and ibrutinib with or without rituximab are category 1, preferred regimens. Acalabrutinib is a category 2A, other recommended treatment option
  - Up to 40% of WM patients may have recurrent mutations in the CXCR4 gene and certain CXCR4 mutations may confer resistance to ibrutinib; therefore, the NCCN guidelines recommend consideration of CXCR4 gene mutation testing for patients being initiated on ibrutinib therapy as a category 2A, useful in certain circumstances recommendation
- No current US guidelines exist for the treatment of erythema nodosum leprosum, hypereosinophilic syndrome, or chronic eosinophilic leukemia

# Oncology, Oral- Hematological – Overview of Disease State

- **Philadelphia chromosome positive (Ph+) ALL**

- Ph+ ALL is rare in pediatric cases of ALL, occurring in approximately 2% of cases. In contrast, approximately 25% of adult cases of ALL are Ph+

- **Treatment**

- The 2.2021 National Comprehensive Cancer Network (NCCN) guidelines recommend incorporation of a tyrosine kinase inhibitor (TKI) in the frontline regimen for Ph+ ALL as an established standard of care for adolescents/young adults and adult patients
  - The TKI may be combined with either chemotherapy or corticosteroids depending on the patient's age and comorbidities
  - TKI options for induction therapy of Ph+ ALL in adolescents, young adults, and adult patients include imatinib (Gleevec), dasatinib (Sprycel), nilotinib (Tasigna), bosutinib (Bosulif), and ponatinib (Iclusig)
  - The NCCN states that dasatinib and imatinib are the preferred TKIs for induction therapy while ponatinib is preferred as part of the hyper-CVAD chemotherapy regimen
  - In addition, the NCCN ALL guidelines also note bosutinib (Bosulif) is an option but state there is limited data for that particular TKI in Ph+ ALL
  - Mutation testing for the ABL gene should be considered as this mutation can confer greater resistance or susceptibility to a particular TKI, and the choice of a specific TKI should also be based on disease-related features
  - Pediatric patients with Ph+ ALL are also candidates for TKI therapy
- The 3.2021 NCCN guidelines for pediatric ALL specifically list combined treatment regimens containing imatinib or dasatinib
  - A study by the Children's Oncology Group (COG) utilizing imatinib for children with Ph+ ALL demonstrated a 5-year event-free survival of 70% (standard error,  $\pm$  12%) which is superior to historical controls prior to the introduction of imatinib

# Oncology, Oral- Hematological

- **Tibsovo (Tibsovo)**

- **August 2021:** Tibsovo is now indicated for the treatment of adults with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test for patients with locally advanced or metastatic cholangiocarcinoma who have been previously treated. It is already indicated for certain adults with a susceptible IDH1 mutation as detected by an FDA-approved test with AML

- **Indication**

- Acute Myeloid Leukemia (AML): Newly-diagnosed AML who are  $\geq 75$  years old or who have comorbidities that preclude use of intensive induction chemotherapy; Relapsed or refractory AML
- Locally Advanced or Metastatic Cholangiocarcinoma: Locally advanced or metastatic cholangiocarcinoma who have been previously treated

- **Warnings and Precautions**

- QTc Interval Prolongation: Monitor electrocardiograms and electrolytes. If QTc interval prolongation occurs, dose reduce or withhold, then resume dose or permanently discontinue treatment
- Guillain-Barré Syndrome: Monitor patients for signs and symptoms of new motor and/or sensory findings. Permanently discontinue treatment in patients who are diagnosed with Guillain-Barré syndrome

- **Dosage**

- 500 mg orally once daily with or without food until disease progression or unacceptable toxicity
- Avoid a high-fat meal

- **Availability**

- Tablets: 250 mg

# Oncology, Oral- Hematological

- **ruxolitinib (Jakafi)**

- **September 2021: FDA approved oral ruxolitinib (Jakafi) for chronic graft-versus-host disease (GVHD) after failure of 1 or 2 lines of systemic therapy in adults and pediatric patients ≥ 12-year-old. (Already indicated for steroid-refractory acute GVHD in the same age groups, and for select patients with myelofibrosis or polycythemia vera**

- **Indications**

- Intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemia vera myelofibrosis and post-essential thrombocythemia myelofibrosis in adults
- Polycythemia vera in adults who have had an inadequate response to or are intolerant of hydroxyurea
- Steroid-refractory acute graft-versus-host disease in adult and pediatric patients 12 years and older
- **Chronic graft-versus-host disease after failure of one or two lines of systemic therapy in adult and pediatric patients 12 years and older**

- **Warnings and Precautions**

- Lipid Elevations: Assess lipid levels 8-12 weeks from start of therapy and treat as needed
- Major Adverse Cardiovascular Events (MACE): Monitor for development of MACE
- Thrombosis: Evaluate and treat symptoms of thrombosis promptly
- Secondary Malignancies: Monitor for development of secondary malignancies, particularly in patients who are current or past smokers

- **Dosage**

- Stratified by indication and possible baseline platelet count (See TCR/PI)

- **Availability**

- Tablets: 5 mg, 10 mg, 15 mg, 20 mg and 25 mg

# Oncology, Oral- Hematological

- **pacritinib (Vonjo)**

- **March 2022: FDA approved Vonjo, a kinase inhibitor with specificity for JAK2 and IRAK1 (without inhibiting JAK1) indicated for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count  $< 50 \times 10^9/L$**

- **Indications**

- **The treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below  $50 \times 10^9 /L$** 
  - **This indication is approved under accelerated approval based on spleen volume reduction**
  - **Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**

- **Warnings and Precautions**

- **Thrombocytopenia: Manage by dose reduction or interruption**
- **Thrombosis: Including deep venous thrombosis, pulmonary embolism, and arterial thrombosis may occur. Monitor for signs, evaluate and treat promptly**
- **Secondary Malignancies: Lymphoma and other malignancies may occur. Past/current smokers may be at increased risk**
- **Risk of Infection: Delay starting treatment until active serious infections have resolved. Observe for signs and symptoms of infection and manage promptly**

- **Dosage**

- **Recommended dosage is 200 mg orally twice daily**

- **Availability**

- **Capsules: 100 mg**

# Oncology, Oral- Hematological

- **FDA Communications**

- **October 2021:**

- The FDA has granted recognition to a partial listing of the first tumor mutation database that is part of the Public Human Genetic Variant Databases: Memorial Sloan Kettering Cancer Center's Oncology Knowledge Base (OncoKB)

# Oncology, Oral- Hematological

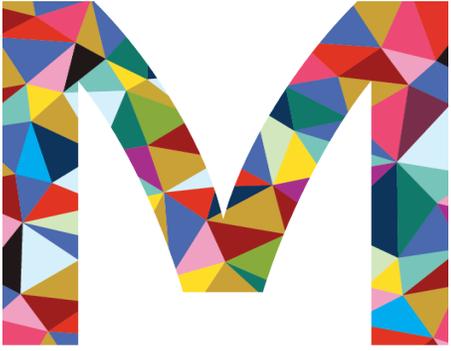
- **Withdrawals**

- **panobinostat (Farydak)- December 2021**

- Secura Bio announced that they will withdraw panobinostat (Farydak) from the US market
    - The drug had received Accelerated Approval for use in combination with bortezomib and dexamethasone for the treatment of patients with multiple myeloma who have received  $\geq 2$  prior regimens, including bortezomib and an immunomodulatory agent
    - Secura stated that they are withdrawing the medication because it is not feasible to complete the required post-approval clinical studies to confirm clinical benefit

- **idelalisib (Zydelig)- April 2022**

- Gilead announced the voluntary withdrawal of indications for the treatment of relapsed follicular B-cell non-Hodgkin lymphoma (FL) and relapsed small lymphocytic lymphoma (SLL) which were approved under an Accelerated Approval based on objective response rates of 54% and 58%, respectively
    - The decision to withdraw these indications is based on an ongoing challenge of enrolling patients in the confirmatory trial
    - Zydelig's indication for relapsed chronic lymphocytic leukemia (CLL) will remain



**Magellan Rx**  
MANAGEMENT<sup>SM</sup>

Magellan Medicaid  
Administration

Oncology, Oral – Breast



# Oncology, Oral- Breast - Overview of Disease State

- ONCOLOGY AGENTS : ANTIMETABOLITES – ORAL
  - Capecitabine
  - Xeloda
  
- ONCOLOGY AGENTS : PHOSPHATIDYLINOSITOL 3-KINASE (PI3K) INHIBITORS – ORAL
  - Piqray
  - **Vijoice**

# Overview of Disease State - Oncology, Oral- Breast

- **Breast Cancer**

- Breast cancer is the most common site of cancer for women in the United States (US), accounting for 30% of all cancer diagnoses, and is second only to lung cancer as a cause of cancer death in American women
- It is estimated that there will be 287,850 new cases of breast cancer diagnosed in the US in 2022 and there will be an estimated 43,250 deaths. The incidence of breast cancer in US women continues to increase by about 0.5% per year
- Known risk factors that may be contributing to this increased incidence of breast cancer include a decline in fertility rates and an increase in body weight. Despite this increasing incidence, death rates from breast cancer have declined by 42% since 1989, largely due to improvements in both early detection and treatment
- The overall 5-year survival for women diagnosed with breast cancer is 90%. Patients who present with localized disease have a 99% 5-year survival rate; however, prognosis for patients presenting with distant metastatic disease is much poorer, with a 5-year survival rate of only 29%
- Breast cancer is most frequently diagnosed in women between the ages of 55 to 74 with the median age at diagnosis being 63 years. Rarely, breast cancer may be diagnosed in men. Other risk factors include various endocrine, genetic, environmental, and lifestyle factors. Some of these risk factors are modifiable, some are not, and the impact of these factors are variable

# Oncology, Oral- Breast

- **alpelisib (Vioice)**

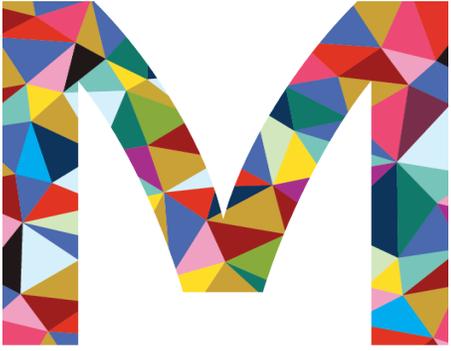
- **April 2022: FDA approved Vioice, a kinase inhibitor indicated for the treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA related overgrowth spectrum (PROS) who require systemic therapy; approved under Accelerated Approval based on response rate and duration of response (DOR), and continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial**
- **Indication**
  - **Treatment of adult and pediatric patients 2 years of age and older with severe manifestations of PIK3CA Related Overgrowth Spectrum (PROS) who require systemic therapy**
  - **This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s)**
- **Warnings and Precautions**
  - **Diarrhea: Can cause severe diarrhea, dehydration, and acute kidney injury. Interrupt, reduce dose, or permanently discontinue treatment based on severity**
  - **Embryo-Fetal Toxicity: Can cause fetal harm. Advise of the potential risk to the fetus and to use effective contraception**
- **Dosage**
  - **Pediatric patients (2 to less than 18 years of age): 50 mg taken orally once daily with food**
  - **Adult patients: 250 mg taken orally once daily with food**
- **Availability**
  - **Tablets: 50 mg, 125 mg, and 200 mg**

# Oncology, Oral- Breast

- FDA Communication

- October 2021:

- The FDA has granted recognition to a partial listing of the first tumor mutation database that is part of the Public Human Genetic Variant Databases: Memorial Sloan Kettering Cancer Center's Oncology Knowledge Base (OncoKB)



# Thrombopoiesis Stimulating Factors

- Hematopoietic Agents: Thrombopoiesis (TPO) Stimulating Proteins





## Growth Factors

- Endocrine and Metabolic Agents: Growth Hormone Releasing Hormones (GHRH)



# Overview of Disease State & Guidelines – Growth Factors

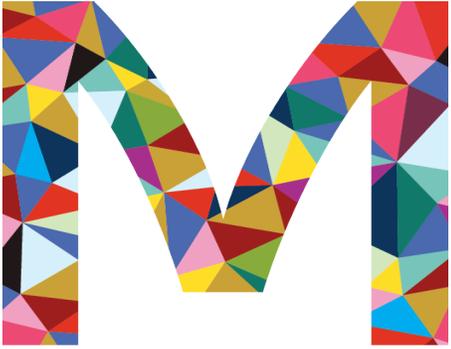
- Achondroplasia

- A genetic bone growth disorder that prevents cartilage from converting to bone and is the most common form of dwarfism
- Is rare, occurring in 1 in every 15,000 to 40,000 live births
- The condition is caused by a mutation of the fibroblast growth factor receptor 3 (FGFR3) gene, which leads to the prevention of normal bone growth
- The average height of an adult with achondroplasia is approximately 4 ft, other characteristics include macrocephaly, bowing of the legs, thoracolumbar kyphosis, small fingers, frontal bossing (specific facial features with a prominent forehead), and mid-face hypoplasia
- Patients with achondroplasia have an increased risk of death in infancy, hypotonia, apnea, obesity, and difficulty walking
- Vosoritide (Voxzogo) is the first FDA-approved therapy to treat achondroplasia in patients  $\geq 5$  years of age with open epiphyses
  - Vosoritide is a human C type natriuretic peptide (CNP) analog
  - It binds to a specific receptor called natriuretic peptide receptor-B (NPR-B) and antagonizes the FGFR3 gene downstream signaling, which results in positive endochondral bone growth while promoting chondrocyte proliferation and differentiation

# Updated Information – Growth Factors

- **vosoritide (Voxzogo)**

- **December 2021: FDA has granted Accelerated Approval to vosoritide, Voxzogo, a C type natriuretic peptide (CNP) analog indicated to increase linear growth in pediatric pts with achondroplasia who are  $\geq 5$  years old with open epiphyses. Accelerated Approval was based on an improvement in annualized growth velocity; therefore continued approval may require demonstration of benefit in confirmatory clinical trials**
- **Indications**
  - **To increase linear growth in pediatric patients with achondroplasia who are 5 years of age and older with open epiphyses. This indication is approved under accelerated approval based on an improvement in annualized growth velocity. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)**
- **Precautions/Contraindications**
  - **Renal Impairment: Not recommended in patients with  $eGFR < 60$  mL/min/1.73 m<sup>2</sup>**
  - **Risk of Low Blood Pressure: Transient decreases in blood pressure have been reported**
- **Dosing**
  - **Ensure adequate food and fluid intake prior to administration**
  - **Recommended dosage is based on patient's weight**
  - **Administer subcutaneously once daily**
  - **Monitor growth and adjust dosage according to body weight. Permanently discontinue upon closure of epiphyses**
- **Formulations**
  - **For injection: 0.4 mg, 0.56 mg, or 1.2 mg lyophilized powder in a single-dose vial for reconstitution**



# Growth Hormones

## - Endocrine and Metabolic Agents: Growth Hormone



# Overview of Disease State & Guidelines – Growth Hormones

- Growth hormone deficiency (GHD)

- Results from inadequate production of growth hormone (GH) and can produce various medical conditions dependent on age
- Adults with GHD may have diminished lean body mass, poor bone density, and a number of physical and psychological manifestations
- GHD can be congenital or acquired in childhood or adult life, in addition to being partial or complete
- The condition is usually permanent and may be an isolated deficiency or occur in association with deficiencies of other pituitary hormones. In most cases, the diagnosis of GHD should be based on results from 2 provocative tests as recommended by the Pediatric Endocrine Society (PES)
- The 2009 American Association of Clinical Endocrinologists Guidelines for Clinical Practice indicates no evidence exists to support any specific growth hormone product over another

# Updated Information – Growth Hormones

- **lonapegsomatropin-tcgd (Skytrofa)**
  - **August 2021: FDA has approved Skytrofa for the treatment of pediatric patients  $\geq 1$  year old who weigh  $\geq 11.5$  kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH)**
  - **Indications**
    - The treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH)
  - **Precautions/Contraindications**
    - Increased Risk of Neoplasm: There are risks of malignancy progression in patients with active malignancy. Monitor patients with preexisting tumors for progression or recurrence
    - Glucose Intolerance and Diabetes Mellitus: Periodically monitor glucose levels in all patients. Doses of concurrent antihyperglycemic drugs in diabetics may require adjustment
    - Hypothyroidism: May first become evident or worsen
    - Pancreatitis: Consider pancreatitis in patients with persistent severe abdominal pain
  - **Dosing**
    - Should be administered subcutaneously into the abdomen, buttock, or thigh with regular rotation of the injection sites
    - The recommended dose is 0.24 mg/kg body weight once-weekly
  - **Formulations**
    - For injection: 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg and 13.3 mg

# Updated Information – Growth Hormones

- **Drug Shortage**

- **Somatropin (Zomacton)- 5/21/2021**

- Ferring has notified Health Care Practitioners of a supply shortage for Zomacton 10 mg due to COVID-19 travel restrictions causing delays in qualifying new filling lines
    - Ferring recommended that Health Care Practitioners stop prescribing Zomacton 10 mg to new patients and transition current patients and future patients to Zomacton 5 mg or to other treatment options
    - They also requested that HCPs and patients to contact Ferring's ZoGo support services

# Appendices



# Guidelines - Oncology, Oral- Breast

- **Endocrine therapy for HR-positive disease**

- According to the NCCN V2.2022 guidelines, endocrine therapy should be considered for nearly all patients with HR-positive disease, regardless of menopausal status, age, or HER2 status of the tumor, with the exception of patients with tumors  $\leq 0.5$  centimeters (cm) where adjuvant endocrine therapy is a category 2B rating
- For patients recommended to receive both adjuvant endocrine therapy and adjuvant chemotherapy, these therapies should be given sequentially with endocrine therapy following chemotherapy
- The NCCN guidelines regarding premenopausal women with HR-positive disease recommend tamoxifen for 5 years, with or without ovarian suppression or ablation or the use of an AI for 5 years plus ovarian suppression or ablation (both category 1)
  - After the initial 5 years of therapy, women who are still premenopausal may consider tamoxifen for an additional 5 years to complete 10 years or consider no further adjuvant endocrine therapy (both category 2A)
  - Women who subsequently became postmenopausal after the initial 5 years of adjuvant endocrine therapy may be treated with an AI for an additional 5 years (category 1) or may continue tamoxifen for an additional 5 years to complete 10 years of adjuvant therapy (category 2A)
  - The NCCN guidelines state that the 3 selective AIs, anastrozole, letrozole, and exemestane, have shown similar anti-tumor efficacy and toxicity profiles in randomized studies in the adjuvant and neoadjuvant settings and that the optimal duration of treatment with AIs in adjuvant setting is uncertain

# Guidelines - Oncology, Oral- Breast

- **Targeted therapy for HER2-positive disease**

- The 2020 ASCO guideline regarding optimal adjuvant chemotherapy and targeted therapy for early breast cancer gives a moderate rating of approval for the use of extended adjuvant therapy with neratinib following trastuzumab in patients with early-stage HER2-positive breast cancer
- ASCO states they preferentially favor the use of neratinib in patients with HR-positive and node-positive disease. ASCO further states that neratinib causes substantial diarrhea and diarrheal prophylaxis must be used; patients who begin neratinib within 1 year of trastuzumab completion appear to derive the greatest benefit; and, at a median follow up of 5.2 years, no overall survival (OS) benefit has been observed for the use of extended adjuvant neratinib
- Likewise, the NCCN guidelines state extended adjuvant neratinib may be considered following adjuvant trastuzumab-containing therapy in HR-positive, HER-2 positive, node positive patients with a perceived high risk of recurrence